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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/560,169	12/09/2005	Kazumi Danjo	Q91343	9404

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EXAMINER	
GREENE, IVAN A	

ART UNIT	PAPER NUMBER
1619	

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01/07/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/560,169	DANJO ET AL.	
	Examiner	Art Unit	
	IVAN GREENE	1619	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 December 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,8-14 and 17-21* is/are pending in the application.

4a) Of the above claim(s) *13,14 and 17-19* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,8-14 and 17-21* is/are rejected.

7)☒ Claim(s) *20* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on _____ is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/09/2005, 03/29/2006, 04/03/2008, and 09/18/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the claims

Claims 1-5, 8-14 and 17-21 are currently pending. Claims 1-5, 8-12, 20 and 21 are presented for examination on the merits.

Election/Restrictions

The foregoing restriction is being done in response to Applicant's amendments to the claims submitted with the Requirement for Restriction dated 09/25/2008 which Applicant replied to with the election of Group(I) in the reply filed on 10/24/2008.

Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

1. Group I, claim(s) 1-5, 8-12, 20 and 21, drawn to a radial spherical crystallization product.

2. Group II, claim(s) 13, 14 and 17-19, drawn to a method of making.

As set forth in Rule 13.1 of the Patent Cooperation Treaty (PCT), "the international application shall relate to one invention only or to a group of inventions." Moreover, as stated in Rule 13.2 PCT, Unity of Invention is satisfied “where a group of inventions is claimed in one and the same international application, the requirement of unity referred to in Rule 13.1 shall be fulfilled only when there is a technical relationship

among those inventions involving one or more of the same or corresponding special technical features."

The expression “special technical features” shall mean those technical features that define a contribution which each of the claimed inventions, considered as a whole makes over the prior art so linked as to form a single general inventive concept --A radial spherical crystallization product comprising needle-shaped projections radiating from the crystal core, wherein a sample component is a pharmaceutical drug or a drug carrier--, does not present a contribution over the prior art, as it is disclosed, and therefore anticipated, by Hanna et al. (US 6,063,138). Hanna et al. further disclose the SEM micrograph of the radial spherical crystallization product, lactose in Figure 5 (see Figure 5 below). As a result, as currently presented, claim 1 does not possess a special technical feature and, as such, unity between the above Groups I and II are broken.

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and the product claims are subsequently found allowable, withdrawn process claims that depend from or otherwise require all the limitations of the allowable product claim will be considered for rejoinder. All claims directed to a nonelected process invention must require all the limitations of an allowable product claim for that process invention to be rejoined.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103 and 112. Until all claims to the elected product are found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowable product claim will not be rejoined. See MPEP § 821.04(b). Additionally, in order to retain the right to rejoinder in accordance with the above policy, applicant is advised that the process claims should be amended during prosecution to require the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder**. Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

3. Claims 13, 14 and 17-19 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected subject matter, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 10/24/2008.

Information Disclosure Statement

The information disclosure statement(s) submitted on 12/09/2005, 03/29/2006, 04/03/2008, and 09/18/2008 were filed before the mailing date of the first office action on the merits. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner where in English.

Priority

The U.S. effective filing date has been determined to be 05/26/2004, the filing date of the document PCT/JP04/07171. The foreign priority date has been determined to be 06/10/2003, the filing date of document JAPAN 2003-165565.

Objections

Claim 20 objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 20 is objected to

because claim 4, from which claim 20 depends, recites --a drug carrier--, however, claim 20 recites --a carrier-- which is a broader limitation.

Rejections

Claim Rejections - 35 U.S.C. 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

1. Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

2. Claim 1 is further rejected because it is unclear what the exact relationship between the limitation –a sample component is a pharmaceutical drug or drug carrier.-- and the "radial spherical crystallization product" of the preamble.

Claim Rejections - 35 U.S.C. 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

1. Claims 1, 3, 4, 5, and 8-12 are rejected under 35 U.S.C. 102(b) as being anticipated by Hanna et al. (US 6,063,18).

2. The rejected claims are anticipated wherein the embodiment is lactose as disclosed in figure 5 below. Claims 9-12 are being treated as product-by-process claims or claims of intended use which do not modify the structure of the invention and are therefore properly included in the rejection.

Applicant claims

Applicant claims a radial spherical crystallization product comprising needle-shaped projections radiating from the crystal core, wherein a sample component is a pharmaceutical drug or a drug carrier. Applicant further claims the radial spherical product having a bulk density of 100 mg/mL or less. Applicant further claims the radial spherical crystallization product wherein the drug carrier is a sugar or sugar alcohol.

Hanna et al. disclose a method and apparatus for the formation of particles which allows for a high degree of control over the size, shape, crystalline form and other physico-chemical properties (abstract). Hanna et al. further disclose lactose is commonly used as a carrier for pharmaceuticals, in particular for drugs delivered by inhalation (col. 3, lines 2-5). Hanna et al. further disclose Examples 1 and 2 in which crystalline lactose particles are formed using carbon dioxide as a supercritical fluid (col. 18, lines 64-67; col. 19, lines 1-58). Hanna et al. further disclose the SEM micrograph of the radial spherical crystallization product, lactose in Figure 5.

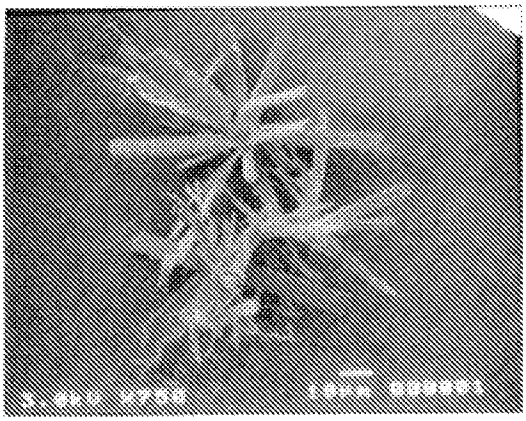

FIG. 5

As to the claimed bulk density, where the claimed prior art products are substantially identical in structure or composition or are produced by identical or substantially identical processes a prima facie case of either anticipation or obviousness has been established. Absent evidence to the contrary the prior art composition must posses the claimed bulk density since it is substantially identical to the claimed composition. See MPEP 2112.01.

3. Claims 1, 3, 4, 5, and 9-12 are rejected under 35 U.S.C. 102(b) as being anticipated by Reverchon et al. (Powder Technol., 114, pp. 17-22).

4. The rejected claims are anticipated wherein the embodiment is salbutamol as disclosed in figure 3 below. Claims 9-12 are being treated as product-by-process claims or claims of intended use which do not modify the structure of the invention and are therefore properly included in the rejection.

Reverchon et al. disclose the micronization of salbutamol by supercritical antisolvent (SAS) precipitation (abstract). Reverchon et al. further disclose the SAS

experiments using supercritical CO2 and a pure liquid solvent with a fixed ratio of CO2/liquid solution (20:1) and fixed liquid flow rate (1 mL/min) and temperature (40°C) while pressure, solution concentration and the type of solvent used were varied one at a time (p. 18, col. 2, lines 12-17 & 50-56). Reverchon et al. further discloses the radial spherical crystallization product comprising salbutamol produced by SAS at 150 bar and a concentration of 10 mg/mL using a dimethylsulfoxide solvent system (p. 20, col. 2, lines 1-9; Figure 3).

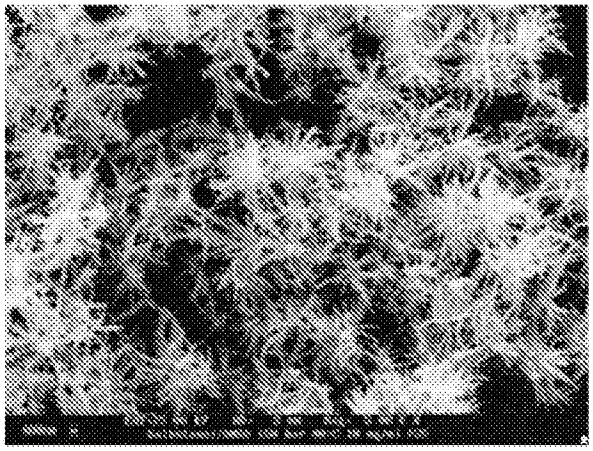

Fig. 3. SEM image of star-like salbutamol particles precipitated by SAS from DMSO at 150 bar, 40°C, 10 mg/ml. At higher concentrations, salbutamol particles tend to form more structured morphologies.

As to the claimed bulk density, where the claimed prior art products are substantially identical in structure or composition or are produced by identical or substantially identical processes a prima facie case of either anticipation or obviousness has been established. Absent evidence to the contrary the prior art composition must posses the claimed bulk density since it is substantially identical to the claimed composition. See MPEP 2112.01.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

1. Claims 1-5, 8-12, 20 and 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hanna et al. (US 6,063,18) and Reverchon et al. (Powder Technol., 114, pp. 17-21) and Yianneskis et al. (US 5,975,076) and Radhakrishnan et al. (US 5,192,528).

2. Claims 1 and 4 are rejected as being obvious over the embodiment(s) wherein the claims are not anticipated (i.e. the product is not lactose or salbutamol, as discussed above). Claims 8-12 are being treated as product-by-process claims or claims of intended use which do not modify the structure of the invention and are therefore properly included in the rejection.

Applicants Claims

Applicant claims a radial spherical crystallization product comprising needle-shaped projections radiating from the crystal core, wherein a sample component is a pharmaceutical drug or a drug carrier. Applicant further claims the radial spherical crystallization product wherein the aerodynamic diameter ranges from 0.1 μm to 20 μm and the bulk density is 100 mg/ml or less. Applicant further claims the radial spherical crystallization product wherein the drug carrier is a sugar or sugar alcohol. Applicant further claims a dry powder inhaler comprising the radial spherical crystallization product.

Determination of the scope and content of the prior art

(MPEP 2141.01)

Hanna et al. teach a method and apparatus for the formation of radial spherical crystallization particles of lactose formed using carbon dioxide as a supercritical fluid, as discussed above. Hanna et al. further teach that it is generally known that other sugars and many amino acids and proteins suffer from similar disadvantages to that of lactose such as low solubility in organic solvents and supercritical fluids/modified supercritical fluids and cannot therefore be formed into particles using former supercritical fluid particle techniques (col. 3, lines 18-30). Hanna et al. further teach the substance used in the invention may be any substance which needs to be produced in particle form, for example lactose and other sugars, proteins, hydrophilic enzymes and inorganic materials (col. 6, lines 29-31 & 36-38). Hanna et al. further teach the substance from which particles are formed is for use in, or as, a pharmaceutical (col. 6, lines 41-43).

Hanna et al. further teach the substance may be a single or multicomponent form (col. 6, lines 50-54). Hanna et al. further teach the supercritical fluid may be any supercritical fluid (col. 6, lines 66-67) and may contain one or more modifiers such as methanol, ethanol, isopropanol, or acetone among others (col. 7, lines 7-9). Hanna et al. further teach the control of parameters such as size, size distribution, shape and crystalline form in the particulate product will be dependent upon the operating conditions used when carrying out the method of the invention (col. 9, lines 64-67) and in particular the flow rates of the supercritical fluid and/or the solution or suspension and/or the second vehicle, into the particle formation vessel may be controlled so as to achieve a desired particle size, size distribution, shape and/or form (col. 10, lines 29-32). Hanna et al. further teach the examples 1 & 2 using lactose, example 3 using maltose, example 4 using trehalose, example 5 using sucrose, example 6 using salmeterol xinafoate, and example 7 using the protein R-TEM beta-lactamase (see Examples cols. 19-21).

Reverchon et al. teach the micronization of salbutamol by supercritical antisolvent (SAS) precipitation, as discussed above.

Yianneskis et al. teach salbutamol sulfate/lactose particles were for use in an dry powder inhaler (abstract; col. 5, lines 25-30).

Radhakrishnan et al. teach a method for delivering a therapeutic dosage of corticosteroid drug to the lungs (abstract). Radhakrishnan et al. teach particle sizes necessary to deliver to the lungs of a patient (col. 1, lines 2 lines 25-30; Figure 1).

Ascertainment of the difference between the prior art and the claims

(MPEP 2141.02)

The difference between the rejected claims and the teachings of Hanna et al. is that Hanna et al. does not expressly teach a dry powder inhaler comprising a radial spherical crystallization product nor do they teach the aerodynamic diameter and the density of the product. The deficiency in dry powder inhaler is cured by the teachings of Yianneskis et al. Radhakrishnan et al. teach the particle sizes necessary to deliver drugs to different regions of the lungs.

Finding of prima facie obviousness

Rationale and Motivation (MPEP 2142-2143)

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to produce a radial spherical crystallization product, as suggested by Hanna et al., and produce the instant invention because the radial spherical crystallization product would provide for a more efficient delivery of drug substance where the desired particle size, size distribution, shape and form can be controlled. The product would especially be useful when used with a suitable inhaler device.

With regards to the aerodynamic diameter Hanna et al. clearly teach that the size of the particles produced using their invention can be controlled. Regarding the bulk density, where the claimed prior art products are substantially identical in structure or composition or are produced by identical or substantially identical processes a prima facie case of either anticipation or obviousness has been established. Absent evidence

to the contrary the prior art composition must posses the claimed bulk density since it is substantially identical to the claimed composition. See MPEP 2112.01.

In light of the forgoing discussion, the Examiner concludes that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a).

The results shown in the examples are not unexpected because, Hanna et al. clearly teach the parameters of particle size, size distribution, shape and form can be controlled using their method, as discussed above. The results shown simply confirm the teachings of Hanna et al.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Conclusion

Claim 20 is objected, Claim 1 is rejected under 35 U.S.C. 112 second paragraph, Claims 1 and 4 are rejected under 35 U.S.C. 102(b), and Claims 1-5, 8-12, 20 and 21 are rejected under 35 U.S.C. 103(a). No claims allowed at this time.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to IVAN GREENE whose telephone number is (571)270-5868. The examiner can normally be reached on Monday through Thursday 7AM to 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on (571) 272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

IVAN GREENE
Examiner, Art Unit 1619

/Johann R. Richter/
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